REMARKS/ARGUMENTS

Claims 1-16 remain for consideration. The Examiner has withdrawn claims 17-39 from consideration as a result of a restriction requirement.

I. NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING

The Examiner has provisionally rejected Claims 1-16 for judicially created nonstatutory obviousness-type double patenting, asserting that the presently claimed invention is not patentably distinct from Claims 17-41 of copending Application No. 11/611,997.

The Applicants respectfully note the Examiner's provisional nonstatutory double patenting rejection. However, the invention of copending U.S. Patent Application No. 11/611,997 is patently distinct from the instant invention. Specifically, U.S. Patent Application No. 11/611,997 requires the presence of a fenicol carbonate, which is patentably distinct from the presently claimed invention. Thus, reconsideration and withdrawal of this provisional obviousness-type double patenting rejection is respectfully solicited.

II. THE PRESENT INVENTION IS NOT OBVIOUS

Claims 1-16 are rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,653,288 (hereinafter "Beuvry et al.") in view of U.S. Patent No. 5,773,422 (hereinafter "Komer") and U.S. Patent No. 5,082,863 (hereinafter "Apelian et al."), and in further view of Ogunrinade et al. The Applicants respectfully traverse the Examiner's rejection. The present invention is not obvious in view of the cited references.

As stated in the MPEP, §706.02(j), three criteria must be met to establish a prima facie case of obviousness. First, there must be some suggestion or motivation to modify a single reference or to combine the teachings of more than one reference. Second, there must be a reasonable expectation of success. Third, the modified prior art reference or combination of references must teach or suggest all the claim limitations. Each of the first and second criteria can not be based on applicant's disclosure, but must be found in the prior art, or based on the knowledge generally available to one of ordinary skill in the art.

The Office Action alleges that Beuvry et al. teaches an injectable composition comprising ivermectin. Applicants respectfully submit that Beuvry et al., whether considered

alone or in combination with the additional cited references, quite simply does not teach the claimed invention and that withdrawal of the rejection is warranted.

Beuvry et al. does not disclose, teach or suggest anything about an injectable composition comprising a compound of Formula I (*e.g.*, florfenicol) and an endectocidic compound (*e.g.*, ivermectin). Beuvry et al. only generally mentions that "other bioactive agents such as antibiotics" may be included. (Col. 13, lines 41-49). Such open-ended language, however, cannot constitute a prima facie showing of obviousness as to Applicants' claims 1-16. In fact, such a generic description is insufficient to support a showing of obviousness. *See Takeda Chem. Indus. v. Alphapharm*, 2007 WL 1839698, *4-*11, 83 USPQ2d 1169, 1174-79 (Fed. Cir. June 28, 2007). Moreover, given Beuvry et al.'s teaching toward formulations comprising ivermectin and the lack of teaching toward formulations comprising ivermectin in combination with compounds of Formula I, a skilled artisan reading the cited art would have had no motivation to go beyond using ivermectin.

In *Takeda*, the Federal Circuit established that even in this post-KSR era, art cannot be combined to render a specific combination obvious unless there is some teaching or suggestion in the art pointing toward that specific combination over all the other possible combinations in the art. *See Takeda Chem.*, 83 USPQ2d at 1174-79 (no prima facie obviousness where prior art reference fails to provide motivation for specifically selecting the claimed compound over numerous compounds disclosed in the reference); *see also* MPEP 2143.01(III). As recognized in the Office Action, Beuvry et al. fails to disclose a composition comprising a compound of Formula I and ivermectin. Beuvry et al. only merely provides a general proposition that an antibiotic may be included in an ivermectin formulation. Given the fact that there exist hundreds of different antibiotics, and each one can have different physical, chemical, and pharmacological properties, as well as different antibacterial spectra and mechanisms of action that one must consider when formulating with such compounds (*see* The Pharmacological Basis of Therapeutics, "Antibiotics," at 1172 (3rd printing, 1966) (Exhibit A)), a general statement regarding the possibility of including all antibiotics within a formulation, as seen in Beuvry et al., is impracticable. Furthermore, Beuvry et al. does not include compounds of Formula I in the specific antibiotic classes mentioned in the reference. *See*, col. 13, lines 50-52. In fact, the classes of antibiotics mentioned in Beuvry et al. differ from the class of antibiotics for which compounds of Formula I belong. For example, phenicols (*i.e.*, compounds of Formula I) are structurally different from the antimicrobial antibiotics mentioned in Beuvry et al. And, as shown on page 1334 of the Merck Veterinary Manual, 7th Edition (1991) (Exhibit B), chloramphenicol sodium succinate, which is a

compound structurally related to those compounds of Formula I of the presently claimed invention, is actually shown to be **incompatible** with erythromycin, which is structurally in the same class of compounds as ivermectin (*i.e.*, both are macrocyclic lactones). In view of this and the above, such a general statement, as seen in Beuvry et al., **would not** lead one of ordinary skill in the art to believe that they could combine a compound of Formula I with ivermectin. And, as more fully discussed below, the remaining cited art does not cure this insufficiency. Therefore, reliance on such a generic description is insufficient to support a showing of obviousness. *See Takeda Chem.*, 83 USPQ2d at 1174-79; MPEP 2143.01(III).

As mentioned above, the additional cited art (specifically, Komer and Apelian et al.) also fails to teach, suggest, or provide motivation to one of ordinary skill in the art to formulate a composition comprising a compound of Formula I (*e.g.*, florfenicol) and an endectocidic compound (*e.g.*, ivermectin). Moreover, these references do not cure the insufficiencies of Beuvry et al. Combining two or more fixed-dose actives is not as simple to develop as hindsight provides. *See generally*, The Merck Veterinary Manual, at 1333-1335 (Exhibit B). In fact, it is known in the prior art and within the knowledge of one skilled in the art that combined actives can react with each other, either chemically or physically, thereby making at least one active less bioavailable or the combination toxic or both. *See* The Merck Veterinary Manual, at 1333 (discussing that "the occurrence of drug-drug interactions in the pharmaceutical phase is frequently unpredictable.") (Exhibit B). Just because two or more actives, individually administered, may work in combination in a subject does not mean that they are amenable to assembling in one formulation. *See* The Merck Veterinary Manual, at 1335 ("[t]he general rule to avoid direct drug-drug interactions is simply **not** to mix pharmaceutical preparations before or during their administration unless it is known that the respective formulations are completely compatible.") (Exhibit B). There are inherent problems with this approach owing to, for example, the different molecular weights, structures and solubilities of the actives to be combined, which may differ substantially from each other and thus, pose a challenge regarding formulation. *See* The Merck Veterinary Manual, at 1333 (Exhibit B). For example, in the present invention, compounds such as florfenicol and ivermectin have different structures and functional groups on each molecule, which results in differing solubilities, degradation and stability pathways. These differences must be considered when formulating a combination such as the presently claimed invention. Therefore, because of these chemical and physical differences and the possibility of these compounds reacting when combined, it would not be obvious to one of ordinary skill in the art to combine the florfenicol formulation, as disclosed in Apelian et al., with the ivermectin

formulation, as disclosed in the Beuvry et al. and Komer references. **The Office action has failed to point to any teaching that would have led a skilled artisan wanting to formulate a composition comprising a compound of Formula I of Applicants' application and an endectocidic compound to specifically turn to any of the cited references and arrive at the presently claimed invention.** Moreover, Beuvry merely provides a generic disclosure of the use of antibiotics and in view of the potential vast differences regarding chemical makeup within this class of compounds, such a statement does not provide any teaching regarding formulation of these compounds to one of ordinary skill in the art. *See generally*, The Merck Veterinary Manual, at 1333-1335 (Exhibit B); *see also* The Pharmacological Basis of Therapeutics, "Antibiotics," at 1172 (3rd printing, 1966) (Exhibit A). And, the specific antibiotics that are disclosed in Beuvry et al. differ from those claimed in Applicants' invention. Thus, Applicants request reconsideration of that proposition.

Finally, the Examiner asserts that the Ogunrinade et al. reference "discloses that immunodepression is known to accompany parasitic disease, and co-infection of parasite and bacteria are known in the art." (Office Action at page 4). This rationale, however, is incorrect. In fact, it was known in the art that immunodepression is **not known** to accompany every parasitic infection. *See, e.g.*, Colle, et al., "*Lack of A General Immunosuppression During Visceral Leishmania Tropica Infection In BALB/c Mice: Augments Antibody Response to Thymus-Independent Antigens and Polyclonal Activation*, J. of Immunology, v. 131, pgs. 1492-94 (Sept. 1983) (Exhibit C). Moreover, Ogunrinade et al., itself, recognizes that immunodepression is not known to accompany every parasitic infection. In the introduction section, the author quotes a study by Goose (1977), wherein there was a depression of immune response to *Fasciola hepatica* in rats, but at the same time a "non-specific immunostimulant" effect against trypanosomiases was observed in the same animals. (Ogunrinade, at 121).

In view of the above, the cited references, whether viewed alone or in combination, **fail to provide any teaching, suggestion, or motivation** for one of ordinary skill in the art to arrive at a composition for the treatment of microbial and parasitic infection in an animal comprising a compound of Formula I and an endectocidic compound. Rather, it was Applicants who, in their quest to develop a composition to treat microbial and parasitic infection with a single application, invented such a composition.

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. §103(a) are respectfully solicited.

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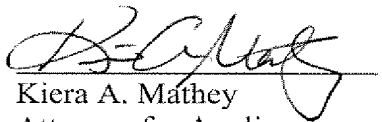
The Applicants believe that the next step in the prosecution of this Application should be in the form of a Notice of Allowance and such action is respectfully solicited.

If the Examiner should have any questions regarding this Response and/or patent Application, he is encouraged to contact the undersigned attorney.

Authorization is provided for the payment of the two-month extension fee. No other fees are believed to arise due to this filing, however, if any other fees are required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 19-0365.

Respectfully submitted,



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